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Division of Synthetic Chemistry
– Synthetic Organic Chemistry –

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Scope of Research

The research interests of this laboratory include the development of advanced molecular transformation, total synthesis of biologically active products, and molecular recognition. Programs are active in the following areas: 1) asymmetric alkylation of carbonyl compounds based on “memory of chirality”, 2) organocatalysis for fine organic syntheses, 3) synthesis of unusual amino acids and nitrogen heterocycles, 4) regioselective functionalization of carbohydrates, and 5) the structural and functional investigation of heterochiral oligomers.

KEYWORDS

Site-Selective Functionalization
Molecular Recognition
Organocatalysis
Dynamic Chirality
Unusual Amino Acid

Selected Publications

Kawabata, T.; Moriyama, K.; Kawakami, S.; Tsubaki, K., Powdered KOH in DMSO: An Efficient Base for Asymmetric Cyclization via Memory of Chirality at Ambient Temperature, *J. Am. Chem. Soc.*, **130,** 4153-4157 (2008).

Kawabata, T.; Jiang, C.; Hayashi, K.; Tsubaki, K.; Yoshimura, T.; Majumdar, S.; Sasamori, T.; Tokitoh, N., Axially Chiral Binaphthyl Surrogates with an Inner N-H-N Hydrogen Bond, *J. Am. Chem. Soc.*, **131,** 54-55 (2009).

Yoshida, K.; Furuta, T.; Kawabata, T., Organocatalytic Chemoselective Monoacylation of 1, *n*-Linear Diol, *Angew. Chem. Int. Ed.*, **50,** 4888-4892 (2011).

Hamada, S.; Furuta, T.; Wada, Y.; Kawabata, T., Chemoselective Oxidation by Electronically Tuned Nitroxyl Radical Catalysts, *Angew. Chem. Int. Ed.*, **52,** 8093-8097 (2013).

Tomohara, K.; Yoshimura, T.; Hyakutake, R.; Yang, P.; Kawabata, T., Asymmetric α-Arylation of Amino Acid Derivatives by Clayden Rearrangement of Ester Enolates via Momory of Chirality, *J. Am. Chem. Soc.*, **135,** 13294-13297 (2013).

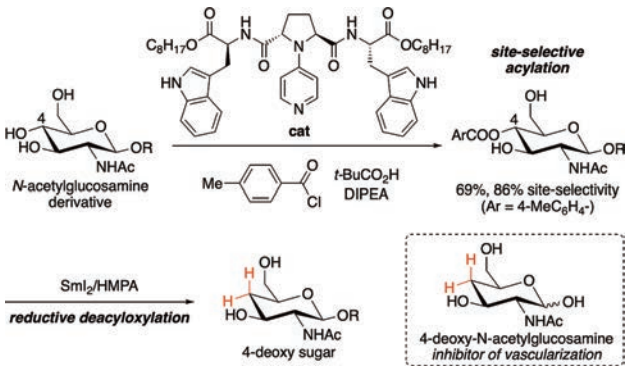
Yoshimura, T.; Tomohara, K.; Kawabata, T., Asymmetric Induction via Short-Lived Chiral Enolates with Chiral C-O Axis, *J. Am. Chem. Soc.*, **135,** 7102-7105 (2013).

Takeuchi, H.; Mishiro, K.; Ueda, Y.; Fujimori, Y.; Furuta, T.; Kawabata, T., Total Synthesis of Ellagitannins via Regioselective Sequential Functionalization of Unprotected Glucose, *Angew. Chem. Int. Ed.*, **54,** 6177-6180 (2015).

Ueda, Y.; Furuta, T.; Kawabata, T., Final-Stage Site-Selective Acylation for the Total Syntheses of Multifidosides A-C, *Angew. Chem. Int. Ed.*, **54,** 11966-11970 (2015).

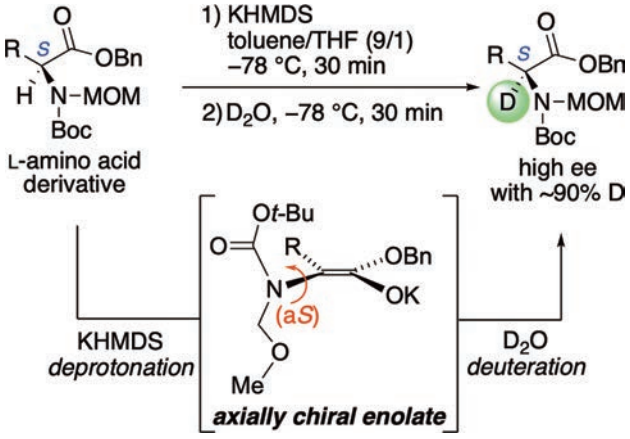
Synthesis of 4-Deoxy Pyranosides via Catalyst-Controlled Site-Selective Acylation Followed by SmI_2-Mediated Deacyloxylation

Deoxysugars have attracted increasing attention because of their biological importance. Their preparation usually required multi-step protection/deprotection sequences, starting from naturally abundant sugars because of the lack of the direct and site-selective manipulation of one of the multiple hydroxy groups of sugar derivatives. We have developed the catalyst which promotes site-selective acylation of the secondary C(4)-OH of glucopyranosides in the presence of the intrinsically more reactive primary C(6)-OH. The site-selectivity was controlled by the catalyst independent from intrinsic reactivity of the substrates; *i.e.*, *catalyst-controlled site-selectivity*. We report here concise synthesis of 4-deoxy pyranosides by reductive deacyloxylation of the 4-*O*-toluoylpyranoses obtained by catalyst-controlled site-selective introduction of the toluoyl group into pyranosides. A representative example of the present protocol includes the synthesis of a 4-deoxy-*N*-acetylglucosamine derivative, possessing inhibitory activity of vascularization, from naturally abundant glucosamine.



Direct Asymmetric Synthesis of α-Deuterated Amino Acid Derivatives via Memory of Chirality

α-Deuterated amino acids have been receiving increasing interests because they play critical roles in mechanistic studies of enzymatic actions and the studies on metabolism of medicinally important compounds. While various methods have been reported for their asymmetric synthesis, there have been no methods reported, in which the parent α-amino acids are employed as the sole source of chirality for the asymmetric induction. In the course of our study on asymmetric synthesis via memory of chirality (MOC), we found that optically active α-deuterated amino acids could be obtained directly from naturally abundant readily available parent amino acids. Treatment of *N*-MOM-*N*-Boc-substituted L-amino acid derivatives with potassium hexamethyldisilazide (KHMDS) at –78°C for 30 min, followed by addition of D_2O as a D source gave α-deuterated L-amino acid derivatives in retention of the configuration and in high ee with ~90% D incorporation. The asymmetric α-deuteration was expected to proceed via axially chiral enolates with a*S* configuration.



Intermolecular Chemo- and Regioselective C-H Amination of Alkoxyarenes Promoted by Dirhodium Nitrenoids

Arylamine motifs are privileged structural units for the development of functional materials and bioactive molecules. One of the most straightforward methods for their synthesis would involve C(sp^2)-H amination of the parent aromatics. We report here intermolecular C(sp^2)-H amination mediated by dirhodium nitrenoids. The reaction proceeded with oxygen-substituted arenes in a chemo- and regioselective manner. The aromatic C(sp^2)-H amination took place at the para position of the oxygen substituent, even in the presence of otherwise more reactive benzylic C(sp^3)-H bonds. The present method was successfully applied to the direct functionalization of calixarene derivative with multiple reactive C(sp^3)-H bonds.